National Toxicology Program
Toxicity Report Series
Number 41

NTP Technical Report on the Toxicity Studies of

1,1,1-Trichlorethane

(CAS No. 76-55-6)

Administered in Microcapsules in Feed to F344/N Rats and B6C3F$_1$ Mice

August 2000

U.S. Department of Health and Human Services
Public Health Service
National Institutes of Health

FOREWORD

The National Toxicology Program (NTP) is made up of four charter agencies of the U.S. Department of Health and Human Services (DHHS): the National Cancer Institute (NCI), National Institutes of Health; the National Institute of Environmental Health Sciences (NIEHS), National Institutes of Health; the National Center for Toxicological Research (NCTR), Food and Drug Administration; and the National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control and Prevention. In July 1981, the Carcinogenesis Bioassay Testing Program, NCI, was transferred to the NIEHS. The NTP coordinates the relevant programs, staff, and resources from these Public Health Service agencies relating to basic and applied research and to biological assay development and validation.

The NTP develops, evaluates, and disseminates scientific information about potentially toxic and hazardous chemicals. This knowledge is used for protecting the health of the American people and for the primary prevention of disease.

The studies described in this Toxicity Study Report were performed under the direction of the NIEHS and were conducted in compliance with NTP laboratory health and safety requirements and must meet or exceed all applicable federal, state, and local health and safety regulations. Animal care and use were in accordance with the Public Health Service Policy on Humane Care and Use of Animals.

These studies are designed and conducted to characterize and evaluate the toxicologic potential of selected chemicals in laboratory animals (usually two species, rats and mice). Chemicals selected for NTP toxicology studies are chosen primarily on the bases of human exposure, level of production, and chemical structure. The interpretive conclusions presented in this Toxicity Study Report are based only on the results of these NTP studies. Extrapolation of these results to other species and quantitative risk analyses for humans require wider analyses beyond the purview of these studies. Selection *per se* is not an indicator of a chemical's toxic potential.

Listings of all published NTP reports and ongoing studies are available from NTP Central Data Management, NIEHS, P.O. Box 12233, MD E1-02, Research Triangle Park, NC 27709 (919-541-3419). Other information about NTP studies is available at the NTP's World Wide Web site: http//ntp-server.niehs.nih.gov.

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Public Health Service
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PEER REVIEW

The draft report on the toxicity studies of 1,1,1-trichloroethane was evaluated by the reviewers listed below. These reviewers serve as independent scientists, not as representatives of any institution, company, or governmental agency. In this capacity, reviewers determine if the design and conditions of these NTP studies are appropriate and ensure that the Toxicity Study Report presents the experimental results and conclusions fully and clearly.

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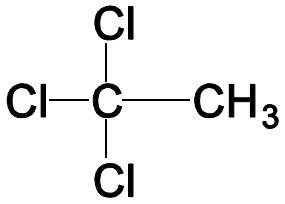
CONTENTS

ABSTRACT



1,1,1-TRICHLOROETHANE

CAS No. 71-55-6

Chemical Formula: $C_2H_3Cl_3$ Molecular Weight: 133.40

Synonyms: Chloroethene; methylchloroform; methyl trichloromethane; α-trichloroethane; 1,1,1-TCE

1,1,1-Trichloroethane is a widely used solvent in industry and in household products such as cleaning agents, wallpaper and carpet glues, carpets, spray and solid insecticides, and rodenticides. 1,1,1-Trichloroethane was studied because of its widespread use in industry and in the home and the potential for human exposure. Groups of 10 male and 10 female F344/N rats and B6C3F$_1$ mice were given 5,000, 10,000, 20,000, 40,000, or 80,000 ppm microencapsulated 1,1,1,-trichloroethane in feed for 13 weeks. Groups of 10 male and 10 female rats and mice served as untreated controls and received feed without microcapsules; additional groups of 10 male and 10 female rats and mice served as vehicle controls and received feed with empty microcapsules. Animals were evaluated for clinical pathology (rats only), reproductive system effects, and histopathology. Genetic toxicity studies were conducted in *Salmonella typhimurium*, L5178Y mouse lymphoma cells, and cultured Chinese hamster ovary cells. In addition, peripheral blood slides from the mice in the 13-week study were analyzed for frequency of micronucleated erythrocytes.

All rats survived to the end of the study. The final mean body weights of exposed rats were within 10% of those of the untreated and vehicle controls. Feed consumption by exposed groups of male and female rats was similar to that by the control groups, suggesting that the diet was palatable to the animals. Based on average feed consumption values, male rats ingested approximately 300, 600, 1,200, 2,400, or 4,800 mg 1,1,1-trichloroethane/kg body weight per day, and females received 300, 650, 1,250, 2,500, or 5,000 mg/kg per day. In general, changes in clinical pathology parameters were minor, sporadic, and inconsistent between

males and females; these differences were not considered to be treatment related or biologically significant. The liver weights of female rats administered 80,000 ppm were significantly less than those of the untreated and vehicle controls. Male rats exposed to 10,000 ppm or greater had a spectrum of nonneoplastic kidney lesions consistent with hyaline droplet nephropathy. No treatment-related gross or microscopic lesions were observed in female rats.

There were no exposure-related deaths in mice. Based on average feed consumption values, male mice ingested approximately 850, 1,770, 3,500, 7,370, or 15,000 mg/kg per day, and female mice received 1,340, 2,820, 5,600, 11,125, or 23,000 mg/kg per day. Even though feed consumption by exposed groups was slightly greater than that by the controls, the mean body weights of male and female mice administered 20,000 ppm or greater were significantly less than those of the untreated and vehicle controls. The heart, kidney, and lung weights of the vehicle control male mice were significantly greater than those of the untreated controls. There were no biologically significant differences in organ weights between exposed and control mice. No gross or microscopic lesions in male or female mice were attributed to chemical exposure.

Epididymal spermatozoal concentrations of male rats and mice given 80,000 ppm were significantly less than those of the vehicle controls.

1,1,1-Trichloroethane was not mutagenic in *Salmonella typhimurium* strains TA98, TA100, TA1535, or TA1537, with or without S9 metabolic activation. In the mouse lymphoma assay for induction of trifluorothymidine resistance in L5178Y cells, 1,1,1-trichloroethane gave a negative response in one test (with and without S9) and an equivocal response in a second test (in the presence of S9). Results of a sister chromatid exchange test in cultured Chinese hamster ovary cells were considered to be equivocal due to an unrepeated questionable response obtained in the presence of S9 in a single trial; without S9, results were negative. 1,1,1-Trichloroethane induced chromosomal aberrations in cultured Chinese hamster ovary cells in the absence of S9; with S9, the increase in aberrations noted in a single trial was not significant. A small increase in the frequency of micronucleated normochromatic erythrocytes was noted in peripheral blood slides from male mice administered 1,1,1-trichloroethane in feed for 13 weeks; the results were determined to be equivocal, while the female peripheral blood micronucleus test results were negative.

In conclusion, 1,1,1-trichloroethane induced nonneoplastic lesions consistent with hyaline droplet nephropathy in male rats. Exposure to 1,1,1-trichloroethane caused decreases in liver weights in female rats and decreases in mean body weights of male and female mice. The no-observed-adverse-effect level (NOAEL) was estimated to be 10,000 ppm for male and female rats and mice.